

WHAT IS CLAIMED IS:

1. A method of identifying an oligomeric compound having bioactivity *in vivo* comprising the steps of:
 - contacting a bioindicative cell with one or more candidate oligomeric compounds *in*
 - 5 *vitro* in the absence of a transfection reagent; and
 - determining whether the bioindicative cell has an altered phenotype, wherein if the bioindicative cell has an altered phenotype, one or more of the candidate oligomeric compounds comprises *in vivo* bioactivity.
- 10 2. A method of claim 1 wherein the oligomeric compound is single stranded.
3. A method of claim 1 wherein the oligomeric compound is double stranded.
4. A method of claim 1 wherein the oligomeric compound is an oligonucleotide,
- 15 peptide nucleic acid, small interfering RNA, micro RNA, micro RNA mimic, or any combination thereof.
5. A method of claim 1 wherein the oligomeric compound is chemically modified.
- 20 6. A method of claim 5 wherein the oligomeric compound is a gapmer.
7. A method of claim 6 wherein the gapmer comprises two 2'-O-methoxyethyl, 2'-O-methyl, 2'-methyl, or 2'-F wings.
- 25 8. A method of claim 1 wherein the oligomeric compound comprises phosphorothioate internucleoside linkages.
9. A method of claim 1 wherein the bioindicative cell is a mammalian tissue-derived cell.
- 30 10. A method of claim 9 wherein the mammalian tissue-derived cell is a primary hepatocyte, primary keratinocyte, primary macrophage, primary fibroblast, primary pancreatic cell, or a stem cell.

11. A method of claim 9 wherein the mammalian tissue-derived cell is a rodent primary hepatocyte.

12. A method of claim 11 wherein the rodent is a mouse.

13. A method of claim 11 wherein the rodent is a rat.

14. A method of claim 9 wherein the mammalian tissue-derived cell is a primate primary hepatocyte.

15. A method of claim 14 wherein the primate is a Cynomolgus monkey.

16. A method of claim 14 wherein the primate is a human.

17. A method of claim 1 wherein the altered phenotype is an increase in uptake of the candidate oligomeric compound, decrease in expression of the mRNA produced from the gene to which the candidate oligomeric compound is targeted, or decrease in expression of the protein encoded by the gene or mRNA to which the candidate oligomeric compound is targeted.

18. A method of claim 1 wherein the candidate oligomeric compound is designed to inhibit gene expression by hybridizing to a target through an antisense mechanism.

19. A method of claim 18 wherein the antisense mechanism is an RNase H-mediated inhibition of the target of the candidate oligomeric compound.

20. A method of claim 18 wherein the antisense mechanism is an RNA interference-mediated inhibition of the target of the candidate oligomeric compound.

21. A method of claim 18 wherein the antisense mechanism is splicing.

22. A method of claim 1 wherein the candidate oligomeric compound is designed to inhibit RNA metabolism by hybridizing to a target through an antisense mechanism.

23. A method of claim 1 wherein the candidate oligomeric compound is designed to inhibit transport by hybridizing to a target through an antisense mechanism.

24. A method of claim 1 wherein the candidate oligomeric compound is designed to
5 inhibit protein metabolism by hybridizing to a target through an antisense mechanism.

25. A kit comprising an assay platform, a bioindicative cell, and a bioactive oligomeric compound.

10 26. A method of identifying an oligomeric compound having bioactivity *in vivo* comprising the steps of:

contacting a primary hepatocyte with a candidate oligomeric compound *in vitro* in the absence of a transfection reagent; and

determining whether the primary hepatocyte has a decreased level of an RNA to
15 which the candidate oligomeric compound is targeted, wherein if the primary hepatocyte has a decreased level of the RNA, then the candidate oligomeric compound comprises *in vivo* bioactivity.

27. A method of identifying a small interfering RNA having bioactivity *in vivo*
20 comprising the steps of:

contacting a primary hepatocyte with a candidate small interfering RNA *in vitro* in the absence of a transfection reagent; and

determining whether the primary hepatocyte has a decreased level of an RNA to
25 which the candidate small interfering RNA is targeted, wherein if the primary hepatocyte has a decreased level of the RNA, then the candidate small interfering RNA comprises *in vivo* bioactivity.